ANEMIA AND ITS CLINICAL CONSEQUENCES IN PATIENTS WITH CHRONIC DISEASES

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Anemia is not considered a serious clinical condition by the vast majority of physicians. Instead, it is thought to be either an insignificant finding in an otherwise healthy patient or a comorbidity that compounds the complexity of managing a patient with ≥1 chronic disease. Although the risks and benefits of treatment for non nutritionally based anemia have been reasonably well documented, the magnitude of risk associated with untreated anemia remains largely unknown.

The contribution of anemia to poor outcomes in chronically ill patients has been documented in many diseases to various degrees.1 In patients with chronic kidney disease, for example, the impact of anemia on morbidity, mortality, and quality of life (QOL) has been extensively examined; numerous publications describing this patient population are available. For other chronic diseases, much less information has been published, and the available publications have not been collated and summarized.

The systematic reviews presented here in contain a synthesis of the growing body of literature on both the prevalence of anemia and the effects of this condition on various clinical and functional outcomes, including mortality, morbidity, and QOL. The articles examine the impact of these issues on 6 key clinical areas: geriatrics, cancer, human immunodeficiency virus (HIV) infection, inflammatory bowel disease (IBD), rheumatoid arthritis, and surgery. (Although the role of anemia in congestive heart failure is gaining interest, the data from this emergent area of research lie beyond the scope of this review.) The evidence in aggregate indicates that anemia is an important, possibly independent, factor determining patient outcomes in these chronic disease states. Moreover, the evidence suggests that there is a critical need for a paradigm shift to the recognition of anemia as an important condition leading to significant consequences when it is not identified and effectively treated.

Anemia, defined by the World Health Organization (WHO) as a hemoglobin concentration <130.0 g/L in men or <120.0 g/L in women, is more common than is generally realized.2 The National Center for Health Statistics provides a conservative estimate, through self-reported data, of approximately 3.4 million Americans with anemia; women, African Americans, the elderly, and those with the lowest incomes exhibit the highest prevalences of anemia.3 Derived from hemoglobin measures in a nationally representative sample, data from the second National Health and Nutrition Examination Survey (NHANES II) show that anemia is most prevalent in infants (5.7%), teenage girls (5.9%), young women (5.8%), and elderly men (4.4%).4

The likelihood of anemia is even greater in certain elderly subpopulations. Prevalence estimates published in the geriatrics literature range from 2.9% to 61%, with the variations stemming from a number of factors: the anemia

definition used, the setting of the study (e.g., hospitalized vs. community-dwelling elderly), and the clinical characteristics of the patients. The literature suggests that among the elderly, anemia is generally more common in men than women, perhaps because the hemoglobin levels used to define anemia are typically higher for men. Also clear from the literature is that the prevalence of anemia increases with age, even in geriatric populations; in fact, a number of studies found a particularly sharp increase in the prevalence of anemia for patients ≥85 years of age. Whereas the association of anemia and adverse outcomes such as weakness, fatigue, and falls is generally acknowledged in the elderly, very few studies have rigorously examined the impact of anemia on clinical, functional, and economic outcomes or on patient satisfaction.

Not surprisingly, the largest body of publications exists for cancer, in part due to the incorporation of the literature across various cancer types. In addition, the role and importance of anemia in cancer, particularly among patients undergoing chemotherapy, has been known for quite some time, so scientific data have been steadily accumulating. Notably, the research examined suggests that anemia is independently associated with a number of adverse clinical outcomes and may, in addition, affect disease progression by diminishing the efficacy of radiation therapy. The common association between cancer stage and presence or degree of anemia further complicates comprehension of the independent impact of anemia on outcomes in patients with cancer; this complexity presents a methodologic challenge that researchers must address so the state of knowledge in this field may continue to advance.

Although anemia is common in individuals infected with HIV, its prevalence depends on the clinical and demographic characteristics of the patients assessed (e.g., HIV stage, age group). The current body of research also suggests that anemia is associated with disease progression and reduced survival and that the highest rates of anemia prevalence are observed in patients with the most advanced HIV disease, i.e., acquired immunodeficiency syndrome. Anemia has also been associated with decreased QOL in patients infected with HIV. Synthesis of the current literature suggests QOL benefits may be gained when anemia is ameliorated, including improvements in physical performance, energy, health satisfaction, and home management.

IBD is associated with multiple potential causes of anemia, including chronic blood loss, folic acid deficiency, chronic inflammation, malnutrition, hemolysis, and the use of hematopoiesis-suppressing medications. Considering all of these etiologic factors, it is not surprising that anemia prevalence is high in patients with IBD, although published estimates vary widely (8.8% to 73.7%). However, only 2 relevant outcomes studies were identified and reported in this supplement—one assessing QOL, and the other examining disease activity. In both studies, anemia is associated with a detrimental impact, yet the paucity of data highlights an important void in the literature and in comprehension of the role of anemia in IBD.

Rheumatoid arthritis serves as a prototypic example of anemia of chronic disease. In rheumatoid arthritis, anemic patients typically have low serum iron levels despite adequate iron stores. Although estimates of anemia prevalence vary, approximately 1 in every 4 patients with rheumatoid arthritis is anemic. Few studies directly quantify the association between anemia and clinical outcomes in this population, but inferences can be drawn from findings of a number of studies that indirectly assessed the impact of anemia by examining changes in outcomes as anemia is managed. Whereas the results of the studies compiled suggest that anemia is associated with a negative impact on both rheumatoid arthritis symptoms and QOL for patients with rheumatoid arthritis, little rigorous research on anemia-related outcomes has been conducted. This gap in the literature is notable because anemia is a common comorbidity in patients with rheumatoid arthritis.

In surgical patients, anemia can be either a preexisting condition or a result of acute perioperative blood loss, including that due to postoperative phlebotomy. As in the other clinical conditions addressed in this supplement, anemia prevalence estimates vary widely in surgical patients depending on the setting of the study, the clinical characteristics of the patient population, and the anemia definitions used. Not surprisingly, anemia is most strongly associated with an increased risk of requiring allogeneic transfusion; the evidence of an association between anemia and other outcomes (e.g., mortality, deteriorating functional status) is both too limited and too inconsistent for definitive conclusions to be made.

Together, these studies demonstrate the prevalence of anemia within diverse patient populations. If anemia had no independent consequences, these data would be of only casual interest and would have no important implications for patient care. However, accumulating data suggest that anemia has an independent impact on a variety of clinical, functional, and economic indicators and that treatment of anemia can improve patient outcomes. Much challenging work remains to be done for the impact of anemia to be fully understood. Of critical importance are studies to elucidate whether the relation between anemia and poor outcomes is an association only or due to a causal link. Even if a causal link is determined, more information is needed from interventional studies to confirm that treatment

of anemia in such cases will lead to improved outcomes. Pending the results of such studies, clinicians should regard the identification, evaluation, and treatment of anemia as an important element in their approach to care of the patient with chronic disease.

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